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Guido Camps, Ralf Veit, Monica Mars, Cees de Graaf, Paul AM. Smeets

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Title: Just add water: effects of added gastric distention by water on gastric emptying and satiety related brain activity

Authors: Guido Camps[a], Ralf Veit[b,c], Monica Mars[a] , Cees de Graaf[a], Paul AM Smeets[a,d]

[a] Division of Human Nutrition, Wageningen University & Research, P.O. Box 8129, 6700 EV Wageningen, The Netherlands

[b] Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Center Munich at the University of Tübingen, Otfried-Müller-Str. 10. 72076 Tübingen, Germany

[c] Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen, Otfried-Müller-Str. 47, 72076 Tübingen, Germany

[d] Image Sciences Institute, University Medical Center Utrecht, Utrecht University, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands

Corresponding author:

Guido Camps, Postbus 8129, 6700EV Wageningen, The Netherlands, +31-317-485393, guido.camps@wur.nl

Names for PubMed indexing: Camps, Veit, Mars, de Graaf, Smeets

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Running head: Brain activation by nutrient and water induced gastric distention

Trial registration: this study was registered with the Dutch Trial Registry under number NTR5507. (http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=5507)

Abstract

Background: Gastric distention contributes to meal termination. There is little research on the neural correlates of gastric distention by food. To date, neural measures have not been obtained concurrently with measurements of gastric distention.

Objectives: 1) To study how offering a small versus a large water load following a standardized nutrient load affects gastric distention over time. 2) To assess associations between satiety experiences and brain activity and the degree of gastric distention.

Method: 19 healthy males (age 22.2±2.5 y, BMI 21.8±1.5 kg/m^2) participated in a randomized crossover study with two treatments: ingestion of a 500-kcal 150-mL liquid meal shake followed by a low (LV, 50 mL) or a high volume (HV, 350 mL) water load. At baseline and three times after ingestion satiety was scored, MRI scans were made to determine total gastric content volume (TGV) and functional MRI scans were made to measure cerebral blood flow (CBF).

Results: TGV was significantly higher for HV compared to LV at all time points ($p < 0.001$) with relative differences between HV and LV of 292±37 mL after ingestion, 182±83 mL at t=15 min and 62±57 mL at t=35 min. Hunger decreased ($p = 0.023$) and fullness increased ($p = 0.030$) significantly more for HV compared to LV. Ingestion increased CBF in the inferior frontal gyrus and the anterior insula, but there were no differences between treatments. There were no significant correlations between appetite ratings and CBF values.

Conclusion: Performing concurrent gastric MRI and CBF measurements can be used to investigate neural correlates of gastric distention. Increased distention did not induce significantly greater brain activation. Future research should further examine the role of the inferior frontal gyrus in satiety.

Key words: gastric distention, gastric MRI, perfusion MRI, gastric emptying, distention, fullness

Abbreviations: CBF, cerebral blood flow; MRI, Magnetic Resonance Imaging; TGV, total gastric volume;

Introduction

In the effort to better prevent obesity, one strategy may be to limit caloric intake. To this end we could strive to promote earlier meal termination (satiation) (de Graaf & Kok, 2010). Satiation can be increased by increased stomach distention (Geliebter, Westreich, & Gage, 1988). When the stomach is distended with a water filled intragastric balloon meal intake is reduced (Saber et al., 2017). This increase in satiation was investigated by Wang et al., who aimed to find neural correlates of gastric distention using fMRI by inflating and deflating an intragastric balloon with water (G. J. Wang et al., 2008). They observed that distention induced brain activation in satiety related brain areas, such as the amygdala and insula.

Spetter et al. showed differences in brain activation and hormone responses between gastric infusion and ingestion (i.e., gastric plus oro-sensory stimulation) of the same 500-mL nutrient load (Maartje S. Spetter, de Graaf, Mars, Viergever, & Smeets, 2014; M. S. Spetter, Mars, Viergever, de Graaf, & Smeets, 2014). Normal ingestion showed increased activity in the thalamus, amygdala, putamen and precuneus compared to matched gastric infusion of the same load. However, gastric emptying was not assessed. Insight in relative gastric distention would provide more detailed information on the associated stomach distention and the rate of gastric emptying, the contribution of which to neural activation is hitherto unknown.

Gastric distention with a balloon and naso-gastric infusion are suitable tools to investigate orosensory and gastric contributions to satiation. However, they are not very naturalistic and the results obtained with such approaches may have limited ecological validity. Also, such approaches do not provide ways to enhance satiation and thereby limit energy intake. Therefore, researchers have used food manipulations to increase gastric distention such as the incorporation of air (Osterholt, Roe, & Rolls, 2007), water (Rolls, Bell, & Thorwart, 1999)

and the addition of gelling fibers (Hoad et al., 2004). However, this introduces a possible confounder, as incorporated air or water inevitably affect the texture of the test food and the eating speed, both of which have been shown to affect satiation (de Wijk, Zijlstra, Mars, de Graaf, & Prinz, 2008; Miquel-Kergoat, Azais-Braesco, Burton-Freeman, & Hetherington, 2015; Weijzen, Smeets, & de Graaf, 2009; Wijlens, Erkner, Mars, & de Graaf, 2015; Zhu, Hsu, & Hollis, 2013a, 2013b; Zijlstra, De Wijk, Mars, Stafleu, & De Graaf, 2009).

The presence of calories slows gastric emptying (Camps, Mars, De Graaf, & Smeets, 2016a; Marciani et al., 2001). Therefore, a possible way to control both orosensory exposure as well as manipulate gastric distention would be to introduce a caloric load first, and then manipulate gastric distention with water. Using water loads is not new: increased water consumption during the day or with a meal has been shown to increase satiety (Daniels & Popkin, 2010; Lappalainen, Mennen, Van Weert, & Mykkanen, 1993; Stookey, Constant, Popkin, & Gardner, 2008). However, the method used in the current paper is more specific, that is the caloric load is ingested first, allowing the subsequently added water to increase stomach distention. A benefit of this approach would be that the eating speed and associated orosensory experience is similar between conditions. Additionally, if – intragestrically - the water remains separated from the nutrient load it would not change caloric density of the nutrient dense liquid and only add pure distention. We hypothesise that water taken with a meal may sieve from the stomach (Camps, Mars, de Graaf, & Smeets, 2016b; Marciani et al., 2012), but this would still create added distention for some time.

The primary aim of this study was to assess what the effect is of offering a small versus a large water load following a standardized meal on gastric distention over time. The secondary

aim was to examine associations between subjective appetite feelings, brain activity and gastric distention.

Participants and Methods

Design

Participants came to our facilities 2 times in a randomized crossover design. Each participant was always scanned on the same time in the morning after an overnight fast. Participants were offered a standardized liquid meal followed by either a small (50 mL, LV) or a large (350 mL, HV) water load in a random and balanced order.

Participants

Nineteen healthy males (age 22.6±2.4 y, BMI 22.6±1.8 kg/m^2) participated. They were recruited by website and flyers around the campus of Wageningen University. A flowchart of the study can be found in **Supplemental Figure 1**. Inclusion criteria were: being male, aged between 18 and 35 y, having a BMI between 18 and 25 kg/m^2, being of self-reported good general health, willing to comply with study procedures, willing to be informed of incidental findings. Exclusion criteria were: unexplained weight loss or gain of >5 kg in the last two months, oversensitivity to any of the food items used in the experiment, any reported pathologies relating to the gastrointestinal tract which might influence results, use of any medications which may influence gastrointestinal function, having any contraindications for undergoing an MRI, not signing the informed consent form, and being employed or studying at the Division of Human Nutrition at Wageningen University.

Potential participants filled out an inclusion questionnaire to screen for eligibility. Subsequently, they attended a screening meeting that included measurement of weight and height and explanation of the study procedures. During screening, potential participants participated in a mock scanner trial to familiarize them with the scan procedures (Lueken, Muehlhan, Evens, Wittchen, & Kirschbaum, 2012). Participants were unaware of the exact

aim of the study; they were only informed about the fact that we were investigating the digestive system and brain activation.

The study procedures were approved by the Medical Ethical Committee of Wageningen University and in accordance with the Declaration of Helsinki (1975) as revised in 2013 (NL48059.081.14). The study was registered with the Dutch Trial Registry under number NTR4573. Results from the HV condition were used in (Camps et al., 2016b).

Written informed consent was obtained from all participants.

Treatments

Both treatments consisted of a meal shake and a water load, offered in a paper cup. The ingredients of the shake were 50 g cream (AH Basic, Albert Heijn B.V. Zaandam, the Netherlands), 53 g dextrin-maltose (Fantomalt Nutricia®, Cuijk, the Nederlands), 8 g vanilla sugar (Dr.Oetker®, Amersfoort, the Nederlands), 30 g whey powder (Whey Delicious Vanilla, XXL Nutrition, Helmond, the Netherlands), and 100 mL water (**Table 1**). The macronutrient composition of the shake resembled a mixed meal with 50% of the energy from carbohydrates, 30% from fat and 20% from protein. The shake was mixed in a container with an internal whisking ball for approximately 30 seconds. The shake was prepared about 15 minutes before intake, and offered at ~18 ºC. It was consumed from a cup, all subjects finished consumption within 40 sec. The subsequent water load was 50 mL for LV and 350 mL for HV. The water was ingested directly following the shake, which all subjects were able to do within 30 seconds.

Scan session procedures

See **Figure 1** for an overview of the scan sessions. After arrival participants provided baseline appetite ratings. Following this, a baseline scan for stomach content and a baseline perfusion

CBF scan of 5 minutes were performed. After this, participants exited the scanner and consumed the shake, followed by the water load. After consumption, participants were positioned in the scanner and stayed there for approximately 50 minutes. During this time we performed gastric MRI scans and obtained appetite ratings at 2, 15 and 35 minutes post ingestion. At 5, 18 and 40 minutes post ingestion we performed CBF scans with a duration of 5, 8 and 5 minutes, respectively. The MRI body coil and 32-channel head coil were exchanged during the session as needed.

Appetite ratings

Subjective appetite ratings were given via the scanner intercom. Participants verbally scored hunger, fullness, prospective consumption, desire to eat and thirst between 1 and 100 points (Noble et al., 2005).

Gastric volume

Participants were scanned with the use of a 3-Tesla Siemens Verio (Siemens AG, Munich, Germany) MRI scanner using a T_2-weighted spin echo sequence (HASTE, 24 6-mm slices, 2.4 mm gap, 1.19 x 1.19 mm in-plane resolution), with breath hold command on expiration to fixate the position of the diaphragm and the stomach. The duration of one scan was approximately 18 seconds. A custom segmentation tool created in MeVisLab (MeVis Medical Solutions AG, Bremen, Germany) was used to manually delineate gastric content - excluding air - on every slice (Kuijf, 2013). Gastric content volume on each time point was calculated by multiplying surface area of gastric content per slice with slice thickness including gap distance, summed over the total slices showing gastric content. The different layers within the stomach were segmented separately and then summed to determine total gastric volume (TGV) (**Figure 2**).

158

159 **Brain activity**

160 *Data acquisition*

161 Cerebral blood flow (CBF) was measured with a 32-channel head coil using perfusion MRI
162 (Pollock et al., 2009) on the same scanner. Images were obtained with a PICORE Q2T ASL
163 sequence, using a frequency offset corrected inversion pulse and echo planar imaging readout
164 for acquisition. A total of 19 axial slices were acquired in ascending order. Each measurement
165 consisted of tag and control images with the following imaging parameters: inversion time
166 (TI), TI1 = 700 ms, TI2 = 1800 ms, repetition time = 2800 ms, echo time = 13 ms, in plane
167 resolution = 3 × 3 mm, field of view = 192 × 192 mm, and flip angle = 90°, with a slice
168 thickness of 5 mm. The first image of the series was used to estimate the equilibrium
169 magnetization of the blood (M0B) to allow for absolute Cerebral Blood Flow (CBF)
170 quantification. At 27 minutes post ingestion a high-resolution T_1-weighted anatomical image
171 was acquired (magnetization-prepared rapid gradient echo (MPRAGE), matrix size = 256 ×
172 256, 192 sagittal slices, 1 × 1 × 1 mm isotropic voxels, TR = 1900 ms, TE = 2.26 ms, TI =
173 900 ms).

174

175 *Image processing*

176 Image processing was performed using functions from the ASLtbx (Z. Wang et al., 2008) in
177 conjunction with SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK) similar to
178 Kullmann et al. (Kullmann et al., 2015). The tag and control ASL images were separately
179 motion corrected and a common mean image was created. Subsequently, the ASL images
180 were coregistered to the anatomical image and smoothed with a 3-dimensional isotropic
181 Gaussian kernel of 6 mm full-width at half-maximum.

Relative CBF maps were generated by subtracting the tag from the control images. The one compartment model was used for absolute CBF quantification (Buxton et al., 1998; Wang et al., 2003) using the following parameters: inversion efficiency (α)=0.95, water partition coefficient (λ)=0.9 ml/g, T1 of arterial blood (T_{1a})=1684 ms. $T1_2$ was incrementally adjusted per slice with 39.5 ms. The anatomical image was normalized using SPM8 unified segmentation, and the resulting parameter file was used to normalize the CBF maps to MNI space retaining 3 × 3 × 5 mm resolution.

Statistical analyses

A Shapiro-Wilk test for normality was performed using SPSS, per time point per treatment on the variables. The data did not significantly differ from a normal distribution. Post-ingestive values were baseline corrected. A linear mixed model with treatment and time as fixed factors and participant as a random factor was performed in SPSS (IBM, Armonk, USA) to test for significant differences between treatments on satiety ratings and TGV. Post hoc Šidák adjusted tests were performed to further examine the main effects in case of a significant interaction. Significance level was set at a p-value of 0.05. Data are expressed as mean±SD unless otherwise stated.

Whole-brain group level analyses were performed in SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK). To investigate CBF changes a full factorial analysis was conducted including the factors treatment (LV, HV) and time (baseline, post ingestion, 15 and 35 min). The threshold for significance was set at a family wise error–corrected (FWE) peak P-value = 0.05. In case of significant clusters, CBF values of the different anatomical areas were extracted using the WFU PickAtlas (Maldjian, Laurienti, Kraft, & Burdette, 2003; Tzourio-Mazoyer et al., 2002) and MarsBaR toolbox (Brett, Anton, Valabregue, & Poline,

2002) (marsbar.sourceforge.net). A second full factorial analysis in SPM was conducted with the addition of TGV as a covariate.

The association between appetite ratings and extracted CBF values was tested by calculating the Pearson correlation coefficient in SPSS.

Results

Satiety ratings

Satiety and thirst ratings over time can be seen in **Figure 3.**

Hunger ratings significantly changed over time ($p = 0.008$) and there was a significant suppressive effect on hunger by HV in comparison to LV ($p = 0.023$). Fullness ratings significantly changed over time ($p = 0.030$) and fullness was significantly increased more by HV ($p = 0.030$). Desire to eat ratings significantly changed over time ($p = 0.004$) and desire to eat was significantly more suppressed by HV ($p = 0.003$). Prospective consumption ratings significantly changed over time ($p = 0.001$) and prospective consumption ratings were significantly more suppressed by HV ($p < 0.001$). Thirst ratings significantly changed over time ($p = 0.003$) and thirst was significantly more suppressed by HV ($p < 0.001$).

There were no significant interaction effects for satiety ratings.

Total gastric volume

A graph of the TGV for both treatments can be seen in **Figure 4**. **Figure 5** shows TGV per treatment, as well as differences in volume of the water and shake layers.

LV TGV was 251±24 mL directly after ingestion, 209±28 mL at t = 15 min and 166±28 mL at t = 35 min. HV TGV was 543±37 mL directly after ingestion, 391±82 mL at t = 15 min and 229±50 mL at t = 35 min.

TGV was significantly changed over time ($p < 0.001$) and TGV was significantly higher for HV ($p < 0.001$). There was a significant interaction between time and treatment for TGV ($p < 0.001$). Post hoc tests revealed TGV was significantly greater for HV compared to LV at all three time points (all $p < 0.001$). Differences between HV and LV were 292±37 mL directly after ingestion, and of 182±83 mL at t=15 min and 62±57 mL at t=35 min.

Brain activation

An overview of significant clusters can be found in **Table 2**. There was no significant main effect of treatment on brain activation. There was, however, a significant main effect of time in the opercular part of the left inferior frontal gyrus (MNI (-57, 17, 22), Z = 5.49, k = 938, P_{fwe} = 0.001). This cluster extended into the triangular and orbital parts of the inferior frontal gyrus. There was a contra-lateral cluster in the triangular part of the right inferior frontal gyrus (MNI (54, 29, 22), Z = 4.81, k = 319, P_{fwe} < 0.001). This cluster extended into the right middle frontal gyrus and the insula.

There was no significant interaction between time and treatment.

There were no significant correlations between appetite ratings and CBF values. There were no significant correlations between TGV and CBF values.

Discussion

Main results

We examined how offering a small versus a large water load following a standardized meal affects gastric distention over time. Gastric MRI data show that TGV was significantly larger for HV over the course of the measurement period. In addition, appetite was suppressed more for HV than for LV. CBF increased over time in parts of the bilateral inferior frontal gyrus and adjacent insula. However, differences between treatments were not significant, although HV tended to increase brain activity at several time points compared to LV.

Our work shows that it is possible to concurrently measure both gastric volume and brain activity. By changing the MRI coils (body coil and head coil) in quick succession we were able to obtain one baseline and three post-ingestive measurements of both gastric content and CBF. To our knowledge this is the first paradigm to allow direct comparison of MRI determined gastric content with neural activation. One effect of the introduction of water after ingestion of the shake was that it did not mix into it (Figure 2). The data indicates that the water ingested after the liquid food stimulus floats on top and empties relative quickly from the stomach. This is in line with other work showing gastric sieving of low caloric watery fluid while retaining more calorie-dense gastric content (Marciani et al., 2012).

In line with our hypotheses activation in the HV condition tended to be higher than that in the LV condition, although the difference was not significant. This may imply that our manipulation was not strong enough to invoke measurable treatment differences. Earlier paradigms that did find a brain response to gastric distention (Maartje S. Spetter et al., 2014; G. J. Wang et al., 2008) used a 500-mLload, however, larger volumes have also been used (Ly et al., 2017). Ly et al. report activation due to distention induced by a balloon in the right

insula, but activation in this area decreased when a nutrient stimulus of the same volume was infused.

Our results show activation in the opercular part of the inferior frontal gyrus, which has also been shown to be associated with gastric stimulation with a liquid meal after a 36-h fast (Del Parigi et al., 2002). Gut hormones such as cholecystokinin, GLP-1, Peptide YY (PYY) and ghrelin are known to affect brain activity (McLaughlin & McKie, 2016; Zanchi et al., 2017). PYY has been implicated in regulating gastric emptying (Savage, Adrian, Carolan, Chatterjee, & Bloom, 1987). Weise et al. report a positive correlation between plasma PYY and right inferior frontal gyrus resting state CBF in the same region that we found responds to distension (Weise, Thiyyagura, Reiman, Chen, & Krakoff, 2012). Interestingly, stable plasma PYY levels have been shown after non-nutrient distention of the stomach (Oesch, Rüegg, Fischer, Degen, & Beglinger, 2006), which is in line with work showing that PYY release is mediated by caloric chime (Essah, Levy, Sistrun, Kelly, & Nestler, 2007). Future work may strive to include PYY plasma measurements to investigate correlations with inferior frontal gyral activation. Additionally, CCK and ghrelin would be interesting appetite hormones that may help to understand associations between gastric distention and brain activity.

Our data show an increase and subsequent decrease in right anterior insula activity after ingestion. There was greater insula activation for HV than for LV although this difference was not significant. Anterior insula activation is associated with visceral and sensory integration (Avery et al., 2017). E.g. the anterior insula is activated by pure gastric distention with an intragastric balloon (G. J. Wang et al., 2008). Previous work has shown that viscerosensation of the stomach tends to be associated with the right insula (Ladabaum, Roberts, & McGonigle, 2007; Stephani, Fernandez-Baca Vaca, Maciunas, Koubeissi, &

Lüders, 2011; Vandenberghe et al., 2007). Our results are consistent with this, as we show significant CBF changes within the right anterior insula over the course of our measurements. However, though HV led to higher CBF values, we did not see the greatest CBF values directly post ingestion which is the moment of greatest distention.

We scanned participants in a supine position; this position is different from real life were gravity also affects gastric emptying, therefore fluid dispersion throughout the stomach may be slower. Stimulating the antral gastric wall has been shown to be important in increasing emptying contractions (Mizrahi, Ben Ya'acov, & Ilan, 2012), and antral stimulation may be different due to the position of the gastric content relative to the body in a supine position. However, in the literature a supine position is common for gastric MRI studies, and studies which compared positions have found similar emptying (Steingoetter et al., 2006). Lastly, in a within-subject design relative gastric emptying differences remain intact (Jones et al., 2006).

Gastric emptying is usually measured over a longer period of time, up to 180 minutes (Hoad et al., 2004; Marciani et al., 2001; Marciani et al., 2012). Our data show that for this combination of a liquid food stimulus and water, the difference in volume between LV and HV declines from 250-300 mL to around 60 mL in the first 35 minutes. This shows that our CBF measurement fell right into the period with the most divergent gastric volumes between the treatments, indicating that with the current paradigm it should have been possible to detect differences between CBF changes. However, the effect may have been too small to be detectable in this sample.

Our paradigm allows concurrent measurement of gastric volume and brain activation. There has been work showing different effects of gastric distention of a balloon versus the same

volume infused as a nutrient rich liquid (Geeraerts et al., 2011). However, there it was unknown for how long the infused nutrients were retained in the stomach, and what the volume of the gastric content was during the concomitant CBF measurements. Our work opens up possibilities to use nutrient load and water combinations as a specific tool for understanding the effect of gastric distention.

Conclusions

This study is the first to employ concurrent interleaved gastric MRI and CBF measurements. Offering a large versus a small water load after a standardized meal significantly increases gastric distention for over 35 minutes and suppresses appetite. A liquid meal with or without an increased intragastric volume of 300 mL water do not differ enough to induce significantly different CBF changes. However, this method is an easy and valid method to increase gastric distention.

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Conflicts of interest: none.

GC, MM, KG and PAMS designed the study, GC conducted the research, GC, PAMS and RV performed the statistical analysis; GC wrote the paper. RV, MM, CdG and PAMS provided feedback, PAMS had primary responsibility for final content.

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Tables

Table 1. Energy content and nutrient composition of the shake.

Ingredients, per 100g shake	
Protein powder, *g*	12.4
Cream, *g*	20.8
Dextrin-maltose, *g*	21.9
Vanilla sugar, *g*	3.3
Water, *g*	41.6
Total, *g*	100
Nutrients, per 100g shake	
Energy[1], *kJ*	1,393
Carbohydrates, *g*	40
Of which mono- and dissacharides	7
Fat, *g*	10
Of which saturated	7
Protein, *g*	20
Fiber, *g*	1.7
Total ingested	
Shake weight, *g*	241
Shake volume[2], *mL*	150
Shake energy, *kJ (kcal)*	2,093 (*500)*

[1]Nutrient composition of the shake resembles a mixed meal, with 50% of the energy load coming from carbohydrates, 30% from fats and 20% from protein.

[2]The shakes for the two treatments were completely similar, but followed by either 50 mL of water (LV) or 350 mL of water (HV), making total consumed volume 200 mL or 500 mL.

Table 2. Whole brain analysis of LV and HV in 19 healthy men[1]

Area	**k**[2]	**MNI**[3]			**Z**	**P_{fwe}**
		x	**y**	**z**		
Inferior frontal gyrus - opercular part L	938	-57	17	22	5.49	0.001
Inferior frontal gyrus - triangular part L		-51	38	7	5.16	0.006
Inferior frontal gyrus - orbital part L		-51	35	-5	5.02	0.012
Inferior frontal gyrus - triangular part R	319	54	29	22	4.81	0.031
Middle frontal gyrus R		48	38	22	4.76	0.039
Anterior insula R		36	14	-11	4.53	0.101

[1] Main effect of time in a 2 x 4 full factorial model with treatment and time as factors, L stands for left hemisphere, R for right hemisphere. [2]cluster size in number of voxels. [3]Voxel coordinates in Montreal Neurological Institute space.

Figure legends

Figure 1.

Overview of one experimental session for one participant.

Figure 2.

MRI images of transverse slices at the height of the liver, shortly after ingestion of the shake. Left: original images. Right: the same slices as shown on the left but with the gastric content delineated manually based on signal strength as indicated by colorization. Water yields high signal in a T_2-weighted scan, and therefore appears bright. A bright watery layer can be observed above the nutrient rich layer. In the HV image the nutrient rich fraction has been marked with an S and the water fraction with a W. In Supplemental Figure 2 an in vitro example of the SEPARATE condition with similar layering can be seen.

Figure 3.

Hunger, fullness, prospective consumption, desire to eat and thirst plotted over time. There were significant differences between treatments for all appetite measures (n = 19).

Figure 4.

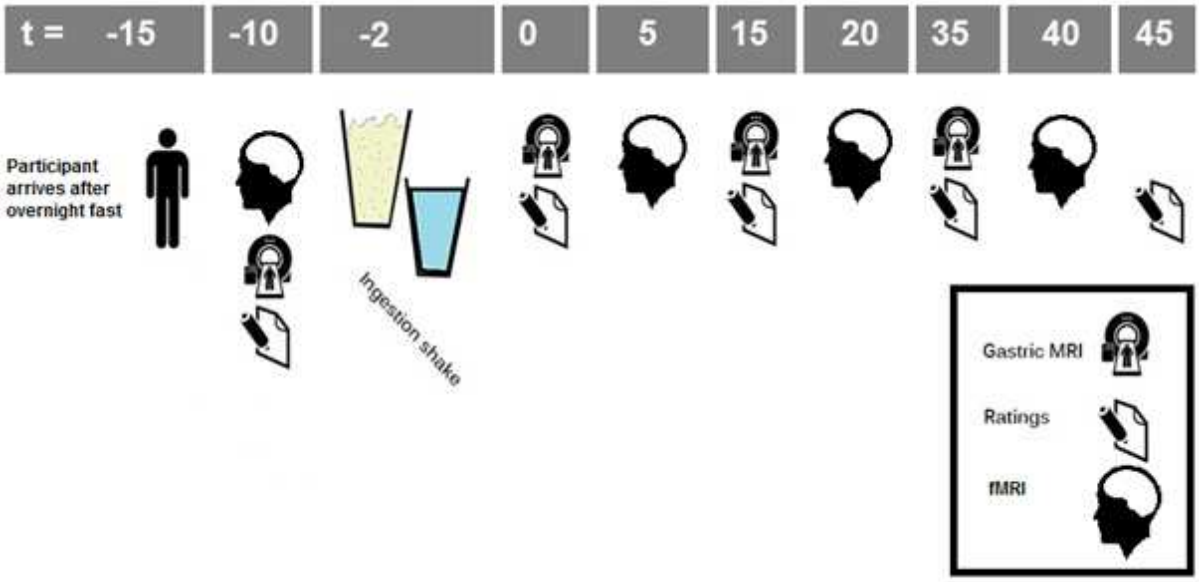
TGV plotted over time. TGV was significantly greater for HV in comparison to LV. TGV at all three time points was significantly different between the treatments (n = 19).

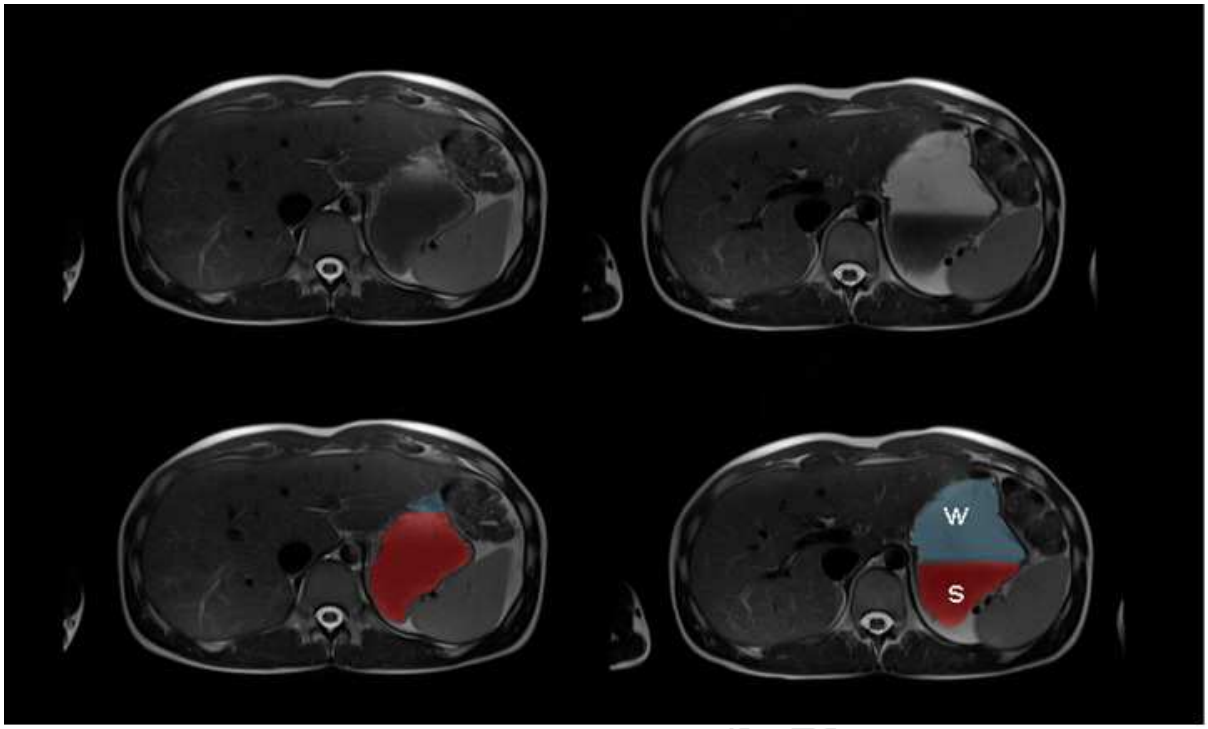
Figure 5.

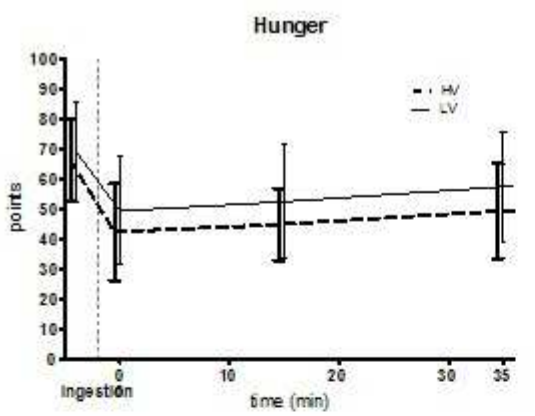
TGV plotted over time, as well as difference between the individual layers within the stomach (n = 19).

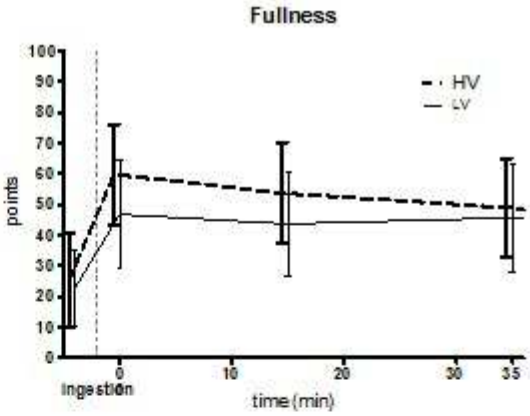
Figure 6.

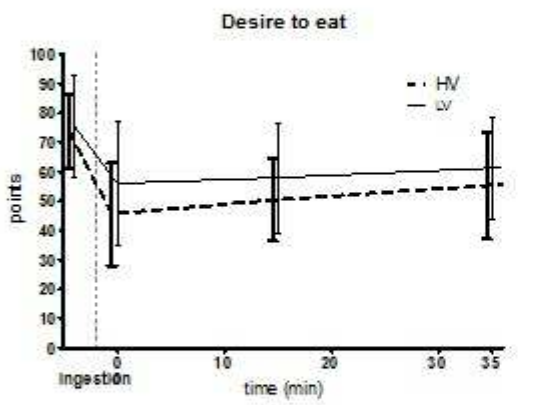
Color coded F-map of the main effect of time overlaid onto study population mean anatomical image (F = 5.72 corresponds to p = 0.001). In the graph: percent CBF deviation from baseline per treatment over time for the bilateral inferior frontal gyrus – triangular part (y = 38) and the right anterior insula (y = 14) (n = 19).

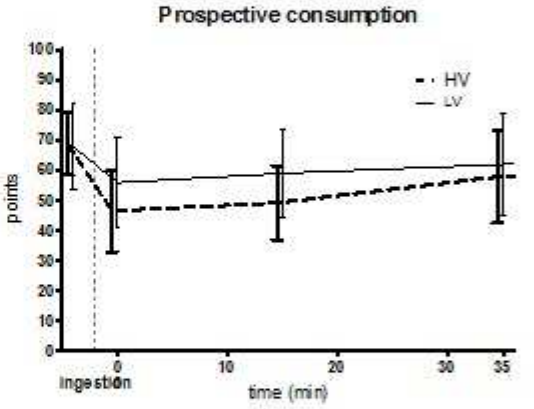


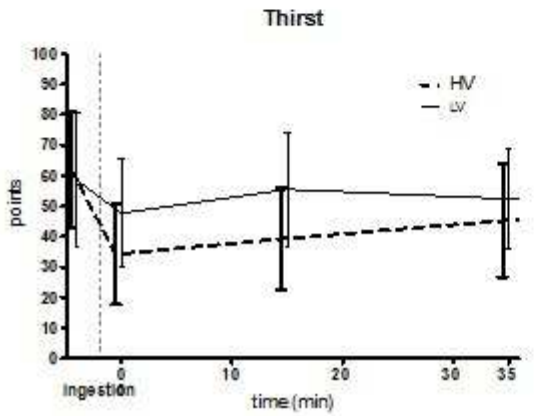


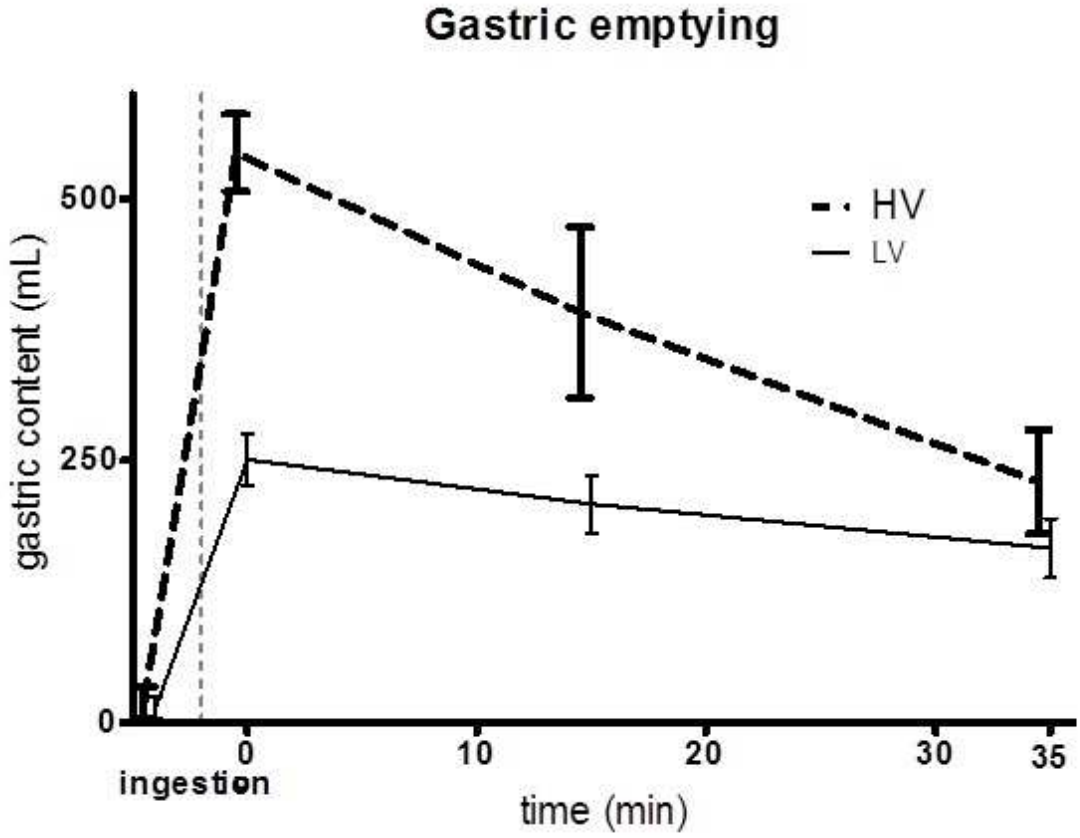

Hunger
HV
LV
points
Ingestion
time (min)

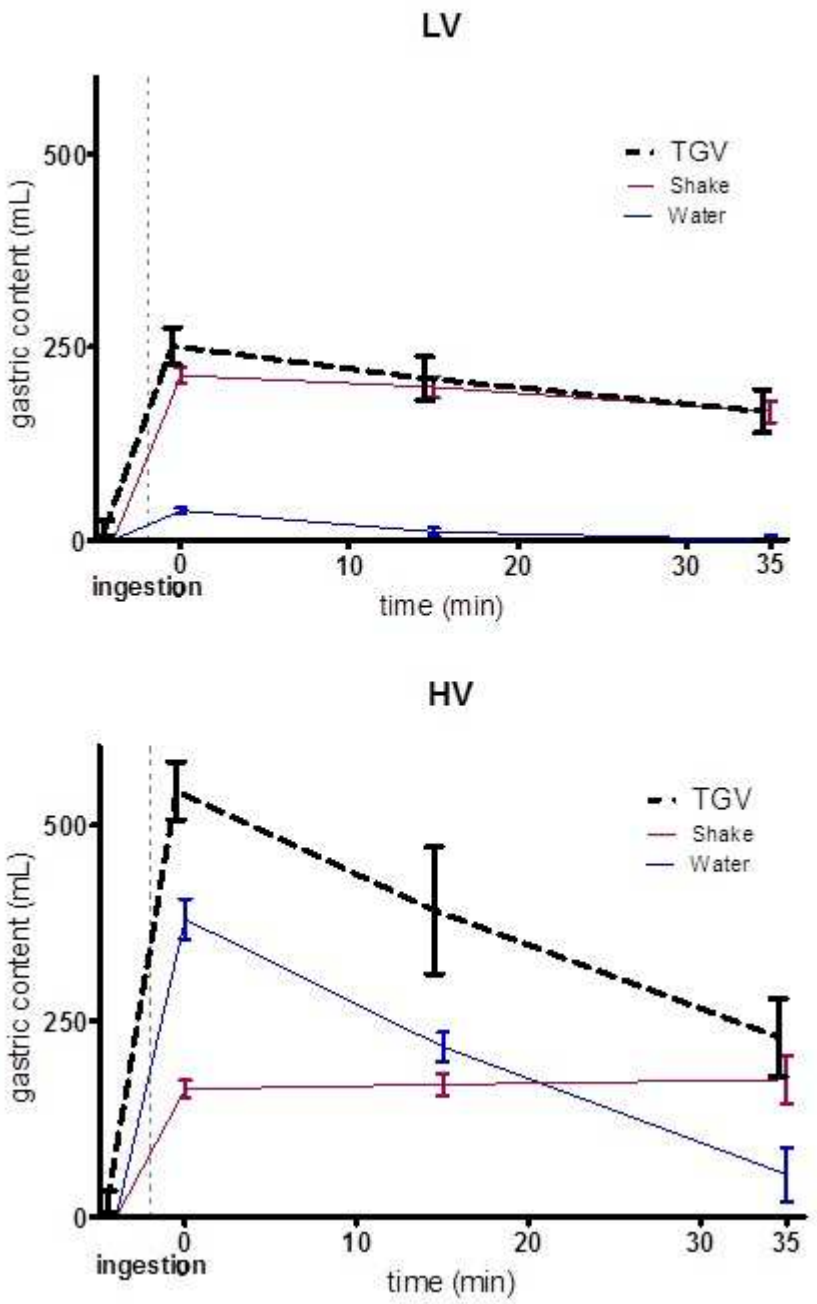

Fullness
HV
LV
points
Ingestion
time (min)

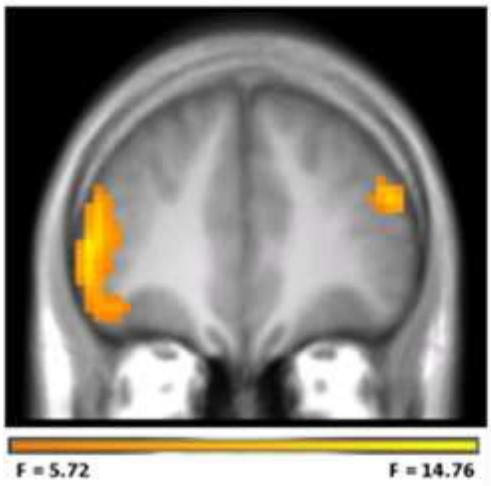

Desire to eat
HV
LV
points
Ingestion
time (min)

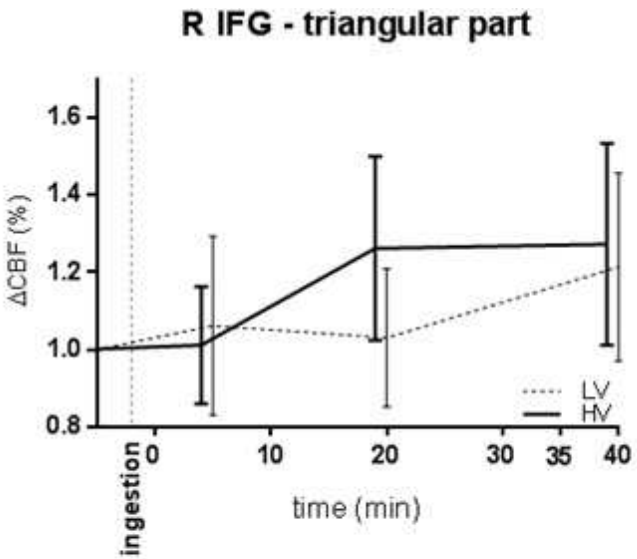

Prospective consumption
HV
LV
points
Ingestion
time (min)

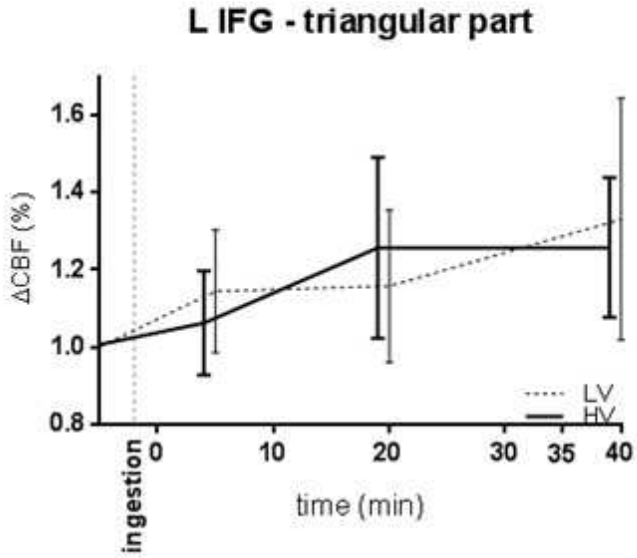

Thirst
HV
LV
points
Ingestion
time (min)

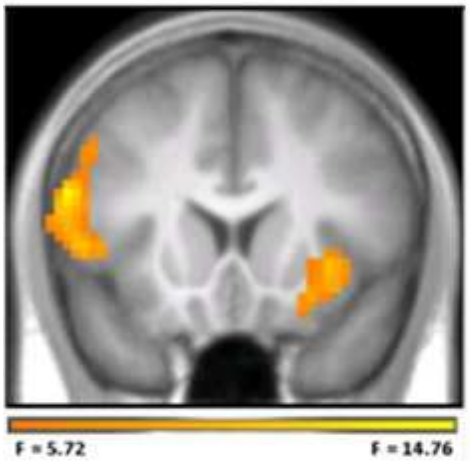



LV
TGV
Shake
Water
gastric content (mL)
500
250
0
ingestion
0
10
20
30
35
time (min)
HV
TGV
Shake
Water
gastric content (mL)
500
250
0
ingestion
0
10
20
30
35
time (min)


F = 5.72
F = 14.76


R IFG - triangular part
ΔCBF (%)
1.6
1.4
1.2
1.0
0.8
ingestion
0
10
20
30
35
40
time (min)
LV
HV


L IFG - triangular part
ΔCBF (%)
1.6
1.4
1.2
1.0
0.8
ingestion
0
10
20
30
35
40
time (min)
LV
HV


F = 5.72
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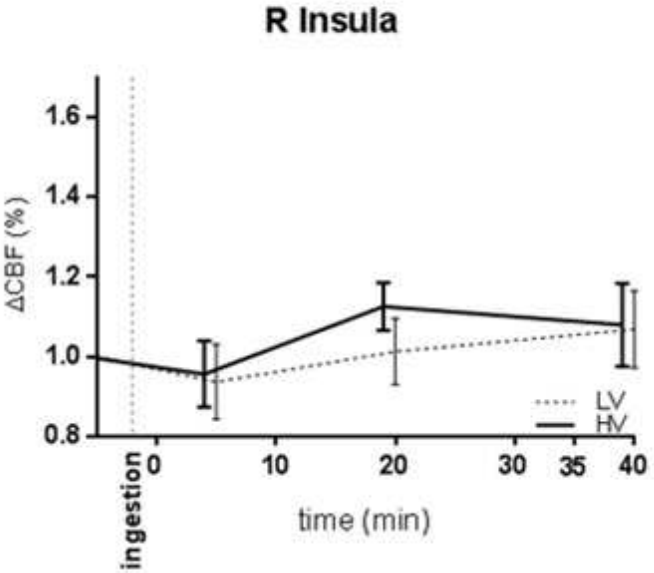
R Insula
ΔCBF (%)
1.6
1.4
1.2
1.0
0.8
ingestion
0
10
20
30
35
40
time (min)
LV
HV